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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/645,426
Filing Date: August 21, 2003
Appellant(s): SEUL, MICHAEL

Eric P. Mirabel
For Appellant

SUPPLEMENTAL EXAMINER'S ANSWER

This is in response to the appeal brief filed September 15, 2006 appealing from the Office action mailed September 11, 2006.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Serial No. 10/310,173-which is a continuation of Serial No. 09/690,040. The present application is also a continuation of Serial No. 09/690,040.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: Claim 31 is stated by Appellant to be rejected as unpatentable under 35 USC 103(a) over Margel in view of Singer. However, claim 31 is a cancelled claim.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Margel (US 5,652,059) July 29, 1997.

Singer et al. (US 5,573,909) November 12, 1996.

Nacamulli et al. (US 5,527,710) June 18, 1996.

Gombinski (US 6,297,062) October 2, 2001.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 81-83, "proteins" and "oligonucleotides" lack antecedent basis. If Applicants intend to recite the ligands comprise proteins or oligonucleotides, please clarify.

Claims 81 and 83, please change "An array" to –The array—for proper antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 76-84,86-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margel in view of Singer et al. (5,573,909).

Margel teaches a composition comprising: a) a substrate such as silicon wafer (silicon substrate of claims 84, semiconductor), glass, or wells of Eliza plate in a planar array (col. 11-12, example 31); It is inherent that wells of an Eliza plate are at discrete sites; b) a population of particles randomly distributed on said sites or wells, said population comprises a plurality of different types of particles with chemical or biochemical binding sites/ligands. (see col. 2, line 35-col. 3, line 5; col. 4, lines 25-65). Regarding claim 88, Margel teaches that immobilization is by chemical bonding or physical bonding. (see col. 3, lines 35-36). The ligands are protein/antibody and biological cells. (see col. 1, lines 40-45; col. 3, lines 23-27). Regarding claim 82, since Margel teaches the use of antibody specific for T-lymphocytes, it is inherent that Margel teaches using monoclonal antibodies because monoclonal antibodies are specific for a cell type. Margel teaches that 1,300 picomoles per squared centimeter protein were bonded to each of the supported microsphere system (see col. 11, lines 7-9).

However, Margel fails to teach each type of particle comprises a distinct chemical or biochemical binding site and comprises a unique chemical label; the biochemical binding site comprises a nucleic acid and particles are exposed to a sample containing target analyte.

Singer teaches microparticles having detectably distinct spectral characteristics of a plurality of dyes incorporated into the microparticles that provide a large and effective Stokes shift, wherein in one example a microparticle-labeled probe emits green

fluorescence and another microparticle-labeled probe emits red fluorescence, wherein each microparticle with a distinct spectral characteristic is labeled with a different target complement (biochemical binding sites) to bind with different targets in a sample (claim 89). (see col. 1, lines 32-34, col. 4, lines 37-67, col. 13, lines 53-56; col. 16, lines 54-65). Singer also teaches that the microspheres are polyacrolein or polystyrene and that the target and target complement are antibodies and proteins, respectively. (see col. 13, lines 60-63, col. 16, lines 3 and 31). Singer also teaches that a nucleic acid probe on the microparticles is selective for target nucleic acids. (see col. 14, lines 15-62, col. 16, lines 9-12, and 40-43; col. 18, lines 49-51).

It would have been obvious to one of ordinary skills in the art to modify the composition of Margel with microparticles having distinct spectral characteristics of a plurality of dyes incorporated into the microparticles and each microparticle is labeled with a different target complement for detecting different target materials in a sample, and such target complement is a nucleic acid as taught by Singer, in order to detect one or more variety of target materials including nucleic acids simultaneously and with high sensitivity since both references teach polyacrolein and polystyrene particles that can immobilize antibodies.

Claim 85 is rejected under 35 U.S.C. 103(a) as being unpatentable over Margel in view of Singer as applied to claim 76 above, and further in view of Nacamulli et al. (US 5,527,710).

Margel and Singer have been discussed above.

However, Margel and Singer fail to teach that the substrate is an electrode.

Nacamulli teaches antigen coated magnetic particles (particle-attached ligands) are deposited uniformly onto the working electrode from a flow stream by placing the magnet directly below. Electrochemiluminescent labeled antibodies are added and the labeled antibodies to the antigens on the magnetic bead immobilized on the surface of the electrode. (see col. 3, lines 10-30).

It would have been obvious to one of ordinary skills in the art to use the electrode taught by Nacamulli as a substrate for use in the composition taught by Margel and Singer since Margel teaches that the population of particles can be immobilized on semiconductor substrate and Singer teaches that the particles are encoded with labels such as fluorescent labels which are the same as electrochemiluminescent labels and Nacmulli teaches that detection ECL labels requires as substrate such as an electrode because electrical pulses are needed to apply in order to modulate the ECL output. The ECL signals are useful in monitoring the rates of binding between the proteins/reactants as well as detecting a low concentration of sample.

Claims 91 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margel in view of Singer as applied to claim 76 above, and further in view of Gombinski (US 6,297,062).

Margel and Singer have been discussed above.

However, Margel and Singer fail to teach an article of manufacture composition comprising two or more of any of the array defined in claims 76 to 90; and the location of the array on said substrate in combination with the chemical or physical characteristic indicates the types of ligands therein.

Gombinski teaches a matrix comprising of several arrays comprising particles positioned randomly on those array. (see fig. 2, col. 12, lines 15-31). Gombinski also teaches that the location of the array can be stained with a dye or a label so that it can be identified. (see col. 7, lines 16-20).

It would have been obvious to one of ordinary skills in the art to produce several of the arrays taught by Margel and Singer as suggested by Gombinski to accommodate assays of different types of ligands.

(10) Response to Argument

Regarding the 112, 2nd paragraph rejection for claims 81-83, Appellants argue that these claims are not indefinite because the terms "proteins" and "oligonucleotides" do not lack antecedent basis. Claims 81 and 83 depends from claims 78 and 79 respectively for "proteins" and "oligonucleotides". Appellants also argue that it is unnecessary to change "An" to –The—in claims 81 and 83.

The words "proteins" and "oligonucleotides" in the preamble of claims 81 and 83, "An array of proteins" and "An array of oligonucleotides", respectively are ***inconsistent*** with what is recited in the preamble of claims 76, 78 or 79, "an array of several different particle-attached ligands".

Regarding the rejection under 103 (a) by Margel in view of Singer for claims 76-84 and 86-90:

Argument A: appellants argue that the particles in Margel are not encoded.

Response: Margel is not relied upon for encoded particles. In fact, the encoded particles are taught in the secondary reference, Singer.

Argument B: appellants argue that the particles of Margel are also coated with the same sheep immunoglobulins (sIgG) and are not "different particles encoded with a chemical or physical characteristics that permits identification of the ligand or ligands attached thereto and permits distinguishing of particles having different ligands attached thereto from each other" as required in claim 76.

Response: Margel teaches the particles are coated with different ligands in col. 2, line 35-col. 3, line 5. Margel teaches that the solid substrate having covalent bonds to at least one member selected from sub-groups (a) and (b) namely: a) substantially a single layer of at least one species of microsphere containing residual reactive functions; b) a multiplicity layers of at least one species of microspheres, where adjoining layers are covalently linked together. Covalent bonds referred above is provided by a ligand denoted A and the joining layer may be linked by a connecting ligand B, the ligands A and B may be the same or different from each other. Thus, one microsphere can have a single layer of ligand, and another microsphere can be have multiple layers of different ligands. Thus, there are at least two different microspheres each having different ligands coated thereon.

Argument C: Appellants argue that the particles of Margel are not in " a planar defined area on the surface of a substrate" as required by claim 76. Margel's particles are coated on the surface of Eliza titer plates, and such wells are parabolic.

Response: Margel does not teach the substrate where the particles are coated to be only Eliza Plate. In fact, Margel teaches the substrate, that is coated with particles, to be a glass disc (examples 1, 20), which is planar; or polypropylene film (example 6).

Argument D: Appellants argue that Margel also does not consider recording assay signals from individual microparticles.

Response: the claims as recited are drawn to a composition, not a method of detecting. Therefore, detecting signals from individually microparticle, which is a method step of detecting, is irrelevant to the recited claims. Margel does not have to teach such step because it is not required in the claims.

Argument E: Regarding Singer: appellants argue that: Singer does not teach detection of assay signals and decoding signatures from such microparticles but only a method of labeling and detecting one or more target materials; wherein immobilized targets of interest are contacted with probes attached to fluorescently labeled microparticles and then unbound probes are optionally removed from the sample by washing; For detection of target materials, the sample is illuminated with means for exciting fluorescence in the microparticle-labelled probes. Thus, in this part of Singer, neither the targets nor the probes are individually encoded, but rather, the presence or absence of fluorescence signals emitted by the particles is detected, to indicate the presence or absence or a target decorated with a probe. In other words, if more than one type of particle is present and so illuminated, smears of a plurality of different fluorescent signals cannot be distinguished; only the different signals can be distinguished. Thus, distinguishing encoded microparticles "having different ligands attached thereto from each other" is not suggested or disclosed in Singer, or in the combination of Margel and Singer, and as encoding is not mentioned in either, there is no suggestion of the claimed subject matter.

Response: Appellants seem to argue the method for detection rather than an array composition. However, to address Appellants' argument thoroughly, Appellants' attention is directed to col. 16, line 54-col. 17, line 11, where Singer teaches that : "in one aspect of the invention, microparticles having detectably distinct spectral characteristics are used for each target material, with each individual microparticle being labeled with a different target complement (ligand) (e.g. one microparticle-labeled probe that emits with green fluorescence is used to label or probe for one particular gene sequence and a different microparticle-labeled probe that emits with red fluorescence is used to label a different gene sequence). If the target is distinguished, then the target complement (ligand) that is bound to such target can also be identified. Therefore, Singer teaches that encoded microparticles can be distinguished individually; and that the encoded microparticles having different ligand/target complement attached thereto are distinguishable from each other. Singer teaches that each microparticles are encoded or coated with a mixture of dyes that emits a detectably distinct spectral characteristic. (see teaching above).

Regarding the rejection under 103 by Margel in view of Singer and further in view of Nacamulli for claim 85: Appellants argue:

that Nacamulli fails to suggest encoded, distinguishable particles.

Response: Nacamulli as stated in the rejection is relied upon for the teaching of a semiconductor substrate such as an electrode, not encoded, distinguishable particles. Margel and Singer as explained above teach encoded, distinguishable particles already. One of ordinary skills in the art would have been motivated to combine these references

because electrode provides electrical pulses for modulating ECL output and the ECL signals are useful in monitoring the rates of binding between the proteins/reactants as well as detecting a low concentration of sample. One of ordinary skills in the art would have had reasonable expectation of success in combining these references because Margel suggested that the substrate can be a semiconducting substrate and the electrode in Nacamulli is a semiconducting substrate; and Nacamulli also teaches that microparticles can be coated on the electrode.

Regarding the 103 rejection for claims 91 and 92, Appellants argue that:

Gombinski relates to purification by "separating at least one species of biological entities from a sample solution and does not teach "an array of several different particle-attached ligands, wherein different ligands are attached to different particles and said particles are encoded with a chemical or physical characteristics that permits identification of the ligands attached thereto and permits distinguishing of particles having different ligands attached thereto". Gombinski does not need encoded particles as a species is being separated. The assay is not multiplexed. Appellants also argue that Gombinski does not teach the particles are encoded with a physical or chemical characteristic, and therefore they need to be spatially separated.

Response: Gombinski is relied upon for the teaching of having a matrix comprising several arrays comprising particles positioned randomly on those array. Gombinski also teaches that the location of the array can be stained with a dye or a label so that it can be identified. Thus, if combined with Margel and Singer, the particles would be in discrete location or the arrays on the matrix of Gombinski, and the particles

of Margel combined with Singer are encoded, and therefore they can be spatially identified. Furthermore, if there is teaching of making an array, then it would be obvious to one of ordinary skills to reproduce or make a multiple number of such arrays. Gombinski, if taught that the particles are encoded and coated with different ligands, would anticipate claims 91 and 92. Thus, it is relied upon for the teaching that the particles can be spatially identified in multiples arrays on a matrix for the motivation of accommodating assays of different types of ligands as those taught by Margel in view of Singer. Furthermore, the limitation of claim 92 is a functional or an intended use limitation. Thus, as long as Margel, Singer and Gombinski together teach an array as recited in claims 76 and 91, then one of ordinary skills in the art would be able to indicate the types of ligands therein using the location of each array on said substrate in combination with the chemical or physical characteristics of the particles.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Pensee Do

Patent examiner

December 22, 2006

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